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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5:		a	1) International Publication Number:	WO 92/16208
A61K 31/415	A1	(43	3) International Publication Date:	1 October 1992 (01.10.92)
(21) International Application Number: PCT/GE (22) International Filing Date: 23 March 1992			(74) Agents: GIDDINGS, Peter e SmithKline Beecham, Munde Hertfordshire AL7 IEY (GB)	ills. Welwyn Garden City
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(54) Title: USE OF BENZIMIDAZOLE ANTHELMI	INTIC	IN	THE TREATMENT OF MICROSPO	RIDIAL INFECTIONS
(57) Abstract				
The use of a benzimidazole anthelmintic in the t	treatme	nt o	f microsporidial infection.	,
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USE OF A BENZIMIDAZOLE ANTHELMINTIC IN THE TREATMENT OF MICROSPORIDIAL INFECTIONS

The present invention relates to the use of certain benzimidazole compounds in the treatment of diseases caused by microsporidia organisms, in particular the treatment of diarrhoea in patients infected with human immunodeficiency virus (HIV).

There are more than 500 species of the protozoa microsporidia which infect animals. Until the advent of 10 acquired immune deficiency syndrome (AIDS) human infection was rare and confined to one or two cases of encephalitis and myositis. Now, however, microsporidium infection is common in the small intestine of HIV infected individuals and is thought to cause diarrhoea. In a recent study in 15 the USA a third of patients in whom no other pathogen as a cause of diarrhoea had been uncovered, were found to have microsporidiosis infection in jejunal biopsy material (Human Pathology, 1990, 21(5), 475-81). Very similar figures were 20 recently obtained in a UK study (Peacock et al., J. Clin. Path. 1991, in press). However, positive proof that Microsporidiosis is of pathogenic importance in the development of diarrhoea requires the ability to eradicate this organism with suitable chemotherapeutic agents or, alternatively, the development of suitable animal models. 25 Such suitable chemotherapeutic agents have, until now, not been available.

The present invention fulfils this need and provides in a first aspect, the benzimidazole anthelmintic albendazole, for use in the manufacture of a medicament for use in the treatment of microsporidia infections, in particular in the treatment of microsporidia infection, for example diarrhoeacausing microsporidial infection, in patients infected with the human immunodeficiency virus (HIV).

In a broader aspect, the invention provides a benzimidazole anthelmintic for use in the manufacture of a medicament for use in the treatment of microsporidia infections, in particular in the treatment of microsporidia infection, for example diarrhoea-causing microsporidia infection, in patients infected with the human immunodeficiency virus (HIV).

The term 'benzimidazole anthelmintic' is intended to include any benzimidazole containing agent which is known to act as a broad spectrum anthelmintic. For example, in addition to albendazole, such compounds include fenbendazole, oxibendazole, mebendazole and parbendazole.

15 In a further aspect the present invention provides a method of treatment of microsporidial infection which comprises administration to a subject in need thereof of an effective amount of a benzimidazole anthelmintic, for example albendazole. In particular the invention provides a method for the treatment of microsporidial infection, for example diarrhoea-causing microsporidial infection, in patients infected with the human immunodeficiency virus (HIV).

When used in the present invention, the active agent is formulated in a standard pharmaceutical composition, for example in a tablet composition.

Suitable doses of active agent will be in the range of from 100 to 5000mg per day, the compound being administered in one or more discrete dosage units, once or twice a day, for as long as is necessary to treat the condition and maintain the patient free of infection. The size, frequency and duration of the dosage regimen will, of course, depend on the severity of the infection.

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RESULTS

A study was carried out on 6 HIV infected individuals with diarrhoea and proven microsporidial infection on 5 jejunal biopsy.

The patients were treated with albendazole (400mg, b.i.d.) and within 1 week, 5 of the 6 had had dramatic symptomatic improvement with complete loss of diarrhoea and arrested weight loss. Subsequently, two patients died of non-diarrhoeal causes and of the remaining 4 who completed one month's treatment, two relapsed.

Jejunal biopsies performed following therapy in five of these patients have shown continuing evidence of Microsporidiosis but an apparent maturation arrest so that frequent meronts are seen but mature spores are not.

CLAIMS:

- A benzimidazole anthelmintic for use in the manufacture of a medicament for use in the treatment of microsporidial infection.
 - 2. The use according to claim 1 in which the benzimidazole anthelmintic is albendazole.
- 10 3. The use according to claim 2 in which the patient treated is also infected with human immunodeficiency virus (HIV).
- 4. The use according to claim 3 in which the 15 microsporidial infection is a diarrhoea-causing infection.

INTERNATIONAL SEARCH REPORT

International Application

PCT/GB 92/00522

I. CLASSIFIC	CATION OF SUBJE	CT MATTER (If several dassification a	ymbols apply, indicate all)*	
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		Documentation Searched other to the Extent that such Documents	than Minimum Documentation are included in the Fields Searched ⁸	
III. DOCUM	ENTS CONSIDERE	D TO BE RELEVANT ⁹	12	Relevant to Claim No.13
Category °	Citation of D	ocument, 13 with indication, where appropr	fate, of the relevant passages 14	Wilderin In Cities Live
х		4761 (CHIMETRON) 20 see page 1, left-hand	February	1
P,X	E.K. B	are, volume 3, no. 4, agdades: "Current trea unistic infections in 6, see page 464	TMENT DI	1-4
P,X	number *micro Intern	formation Service, file 91:446850, "Treatment sporidiosis* with albertional Conference on enging Aids; Florence, (vol. 1); 460P. (vol. e	indazole", VII Aids: Science IT. June 16-21, 1991,	1-4
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"A" doc	usidered to be of parti- ilier document but put ag date nament which may thr ch is cited to establis- ution or other special cument referring to a	meral state of the art which is not cular relevance lished on or after the international ow doubts on priority claim(s) or h the publication date of another reason (as specified) a oral disclosure, use, exhibition or r to the international filing date but	To later document published arter the inter- or priority date and not in conflict with cited to understand the principle or the invention "I" document of particular relevance; the ci- cannot be considered novel or cannot be involve an inventive step "document of particular relevance; the ci- cannot be considered to involve an inve- document is combined with one or more ments, such combination being obvious in the art. "A" document member of the same patent for	by anderlying the almod invention considered to almod invention attree step when the pather such docu- to a person skilled
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Category *	Citation of Document, with Indication, where appropriate, of the relevant passages	Relevant to Claim No.
Tategory		
,x	J. Protozool, volume 38, no. 6, 1991, Society of Protozoologists, 1991; E.U. Canning et al.: "In vitro and in vivo investigations of human microsporidia", pages 631-635, see page 634	1,2

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9200522

GB 9200522 SA 57702

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 07/07/92

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